

They who are ignorant and do not know they are ignorant are doomed to perpetual ignorance, unless enlightenment comes from some external source. That stimulus is education. The appreciation of ignorance is the first step to wisdom. The greater the knowledge, the greater the appreciation of the ignorance. This is the wisdom that is offered to Arizona medical students.

The dawning realization that we lack knowledge in a given area can precipitate several actions. Most people experience an initial sense of exhilaration—almost a revelation—and are stimulated to cast the light of intellect into the dark corners. Others are embarrassed, perhaps even intimidated by the new knowledge, and tend to ignore and reject it. They retreat into the comforting shadows of deadening ignorance—intellectual troglodytes.

I suspect the other face of ignorance in medicine is arrogance. I can still recall studying for the American Board of Internal Medicine's written and oral examinations. I hit the books an average of four hours a day for about a year. I had acquired a 5-ft file of "hot articles"—reprints and clipped original editorials from *New England Journal of Medicine*, *Journal of the American Medical Association*, *Annals of Internal Medicine*, *Archives of Internal Medicine*, *American Journal of Medicine*, plus every key article from the past three years. One week before the examination I could reach into that file, pluck any article at random, read the title, and recite the key teaching point(s)—and give a small lecture on the subject. I exuded hubris. There was nothing worth knowing that I did not know about internal medicine. (I believed that if I had failed that examination, I would have decompensated.)

I happened to wander through that pile ten years later. I would estimate that 90% of the information it contained was either hopelessly out of date or downright incorrect. So much for knowledge; make way for ignorance. Yesterday's absolute truth is today's tiresome anachronism. The treadmill never stops running; if you slow down or stop, you move backwards.

The article tickled another thought. I think we have all learned another lesson over the past 30 years. The era of the Herr Geheimrat has passed. He (there were few women) represented the ultimate unimpeachable authority. Enclosed in a kiosk of towering isolation—insulated from criticism by the suffocating cultural structure of the system—he sailed majestically through the wards at the head of a white-coated flotilla of docile supplicants. He pontificated without fear of challenge, much less contradiction. It was a structure designed to institutionalize ignorance and frustrate any attempt at innovation.

It all came apart in the wake of World War II, when the medical knowledge explosion made it impossible (if not ludicrous) to assume that any single person could be the unassailable repository of all clinical knowledge. The system died harder in Europe than in the United States, but the inevitable divvying up of knowledge into specialties, subspecialties, and subsubspecialties was its death knell. Open teaching rounds with dialogue between chief and staff and with the encouragement of challenge and debate were the great American contribution to medical education.

The essay by Witte and co-workers is a gem of good writing and provocative thinking. Some of it is tongue-in-cheek, but their arrow hits the target. The metaphoric lymphatics remain mysterious, even in our current state of "escalating enlightenment," but at least we know we are ignorant.

Next I wish they would find out why it feels so much better to cross one's legs when sitting for long periods, or

what will happen when we dispatch crews to Mars and deprive them of old-friend gravity for three-plus years.

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## Challenges From the Environment

THE DECADE JUST BEGUN could surely be called "the Decade of the Environment." The challenge of pollution-related illness faces us at this moment. Recognizing environmentally associated diseases and treating them effectively are clinical problems whose solutions will need increasing attention for years to come. Depletion of the ozone layer, acid rain, the "greenhouse effect," and ionizing radiation from nuclear energy plants represent problems that are global in scope yet rarely, if ever, noticeably affect individual medical practices. On the other hand, industrial chemical pollution, the "sick building syndrome," and toxic wastes are more localized issues, affecting circumscribed occupational or residential communities. They are examples of the types of problems that now confront the ordinary physician.

In this issue of the *Journal*, Sparks and co-workers report on their investigation of 53 employees of a large aircraft manufacturing company.<sup>1</sup> A physician previously diagnosed these workers as suffering from a "new" disease called the "aerospace syndrome." When examined by a team of experts from various specialties, however, it was discovered that the workers as a group had a condition characterized by anxiety and depression that was not relieved when they left the workplace. They experienced multiple somatic symptoms without evidence of physical illness, so that the authors report them to be "partial somatizers."

The so-called aerospace syndrome apparently fits well into the category of illness previously referred to as "multiple chemical sensitivities."<sup>2</sup> The latter term describes persons who report multiple symptoms when they are exposed to a variety of common substances, such as perfumes, automobile exhaust fumes, household cleaning products, and new clothes. Many of these "chemically sensitive" persons report adverse reactions to several foods and drugs. No diagnostic physical finding or laboratory test characterizes their condition. In many cases the problem seems to be initiated by a known or suspected occupational or environmental chemical exposure. Those who have investigated this problem sharply disagree regarding its cause. Some view the illness as a form of chemical immunotoxicity.<sup>3</sup> Others see the problem as a somatization disorder<sup>4,5</sup> and others as an iatrogenic condition.

The evaluation of the aerospace syndrome reported by Sparks and associates has some definite shortcomings, but it lends support to the concept that psychological origins often can explain multiple symptoms occurring with exposure to low levels of environmental chemicals if the patient's symptoms are not consistent with known toxic properties of the chemical. The authors point out that the employees in this case were using chemicals found widely in modern-day industry. The ambient levels of chemicals in the factory were low. It should be noted, however, that these measurements were made well after the employees first became symptomatic, so it is possible that their exposures to some of these chemicals may have been higher in the past. In fact, some of the workers reported contact dermatitis and mu-

cous membrane irritation that later resolved with the cessation of exposure. The study also lacks an appropriate control population. Investigation of those workers who had the same exposure but did not file complaints of illness would have strengthened the conclusions.

The authors are to be congratulated for carrying out their study under restrictive conditions that limited them from obtaining the data that would have made the investigation ideal. Whenever environmental pollution or workplace safety appears to be a factor in disease, the case is likely to enter the political arena and the courts. Political and legal decisions in matters of health and disease are only as good as the scientific data on which these decisions are based. Therein lies a dilemma for the clinical investigator. Research into occupational and environmental diseases frequently involves epidemiologic methods. A proper investigation of occupational disease is virtually impossible to design and carry out in the face of impending litigation and in an atmosphere of intense media coverage. It is difficult to enroll the control subjects needed for a well-designed study under such circumstances. Both employers and employees have vested interests in the results, and these interests usually conflict. A controlled exposure of subjects in a laboratory to a suspected chemical is often required for a definitive study, but all too often a definitive procedure like this must be rejected because of the specter of liability.

The study reported by Sparks and colleagues raises a second issue—that of laboratory credibility. The workers in this case allegedly had antibodies to formaldehyde, reported by a commercial laboratory that performed blood tests on the workers. When retested in a university medical center research laboratory where the formaldehyde antibody test had originally been developed, the results were negative. Physicians who evaluate and treat occupational illness are approached by certain commercial laboratories offering a variety of tests, including measurements of antibodies to chemicals, lymphocyte surface markers, and blood and urine levels of industrial chemicals, pesticides, and other potentially toxic products. The validity of many of these measurements and the true "normal" ranges are defined poorly, if at all. Yet such tests are being used to diagnose occupational disease.

The present study raises another issue. How do we define a disease or syndrome? Ideally, a disease is defined on the basis of etiology and pathophysiology. Too often, however, patients present to their physicians with complaints and findings for which there is no clear cause or pathogenesis. In the case of the acquired immunodeficiency syndrome (AIDS), a working case definition was set up by a group of experts to define the diagnosis until the causative virus was isolated; today an etiologic diagnosis of human immunodeficiency virus infection is straightforward.

The term "aerospace syndrome" was created by the media because a physician was convinced that a group of commercial aircraft workers suffered a new disease of toxic origin. The naming of a new syndrome in this case was clearly premature, and even the name was inappropriate. It remains to be seen how long this new name will persist. The term "multiple chemical sensitivities" implies both cause and pathogenesis, neither of which is yet supported by any hard data. Nevertheless, these names carry symbolic meaning to patients. Such names could well contribute to a perception of disability that might not be warranted.

The problem of low-level chemical environmental exposure as a cause of illness to an individual, to the work force, and to the community challenges all in medicine. Too few medical investigators, however, have taken up the chal-

lenge. No one will disagree that we live today with human-made pollution. No one will dispute the desirability of a clean environment for reasons of good health and aesthetics. Many diseases that are caused by toxic and microbiologic contaminants in the air, food, and water have been described and studied with rigorous scientific methods. Many physicians active in the field of environmental and occupational medicine, however, find the increasing tendency today to attribute almost any illness or symptom to an environmental toxin without adequate study a disturbing one. There is every reason to think that the problem will get worse. As industry creates and supplies new products that enhance the quality and safety of daily living, workers, consumers, and the general public will be increasingly at risk of exposure to potentially hazardous substances. The present case is a good example. These aircraft workers were involved in the manufacture of a product for making airline travel safer.

The policymakers who must decide how best to maintain a clean environment for the public good need high-quality input from the medical profession. Full cooperation must be effected among the physicians who carry out studies of industrial pollution, the population at risk, their representatives (unions and legislatures), industry, and the judicial system. A litigious society makes this type of cooperation exceedingly difficult. But it is not impossible.

Clearly, physicians must provide leadership by coming up with innovative proposals for pooling the resources of industrial management, unions, and clinical science. This process would in no way restrict a person's right to be compensated for injury or illness caused by someone else's wrongdoing or by occupational illness. We cannot ignore environmental pollution without risking unnecessary disease. Neither can we ignore the basic principles of good medical practice and sound research, subject patients to unsubstantiated diagnosis, and mislead the media without risking unnecessary psychological harm and disability in the work force.

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### Endometrial Cancer—The High-Risk Early-Stage Patient

THE ARTICLE by Fu and co-workers is a comprehensive synopsis of the endometrial cancer problem, touching most of the recent developments in the areas of histogenesis, diagnosis, treatment, and prognosis.<sup>1</sup> I have selected several points in the review to emphasize and enlarge upon.

Although the authors did not use the more current terminology for endometrial hyperplasia (simple or complex with or without atypia), it remains true that the presence of atypia is the identifying feature of a premalignant lesion. Women in whom this form of hyperplasia develops should be managed by hysterectomy, health permitting, unless it occurs during the reproductive years. In most cases atypical hyperplasia, once manifest, is reversible by high-dose progestins but is incurable. Thus, the risk for cancer persists